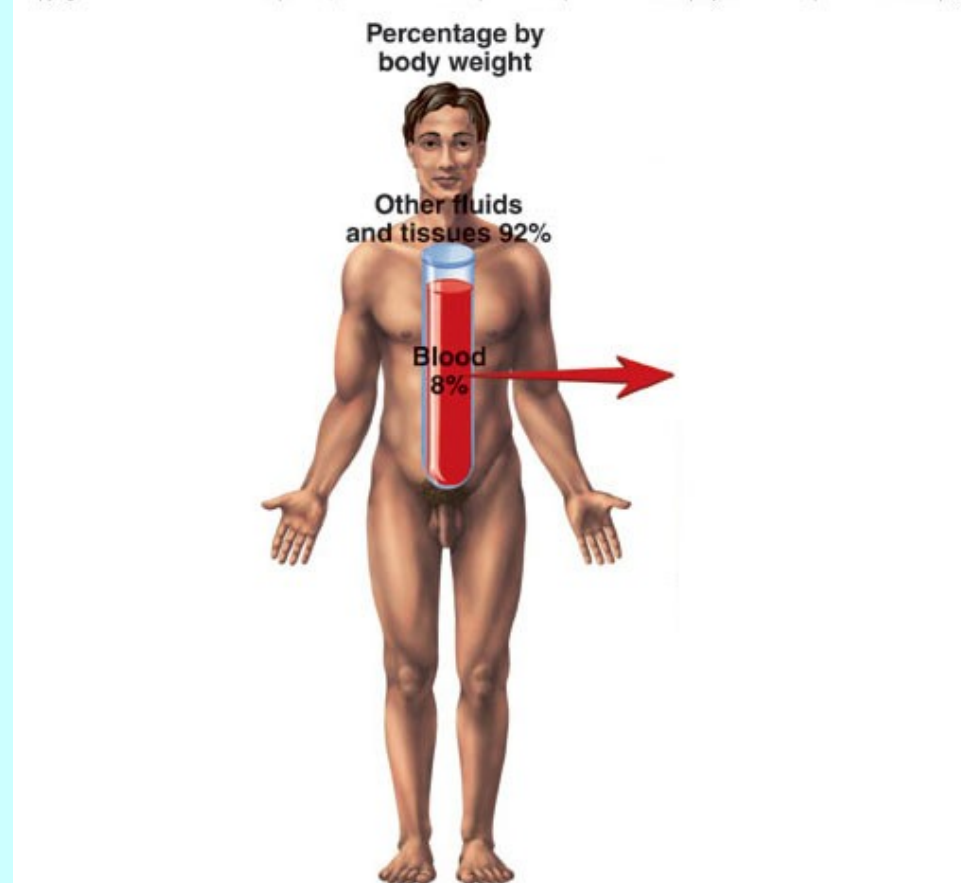


# Cardiovascular System

## Blood

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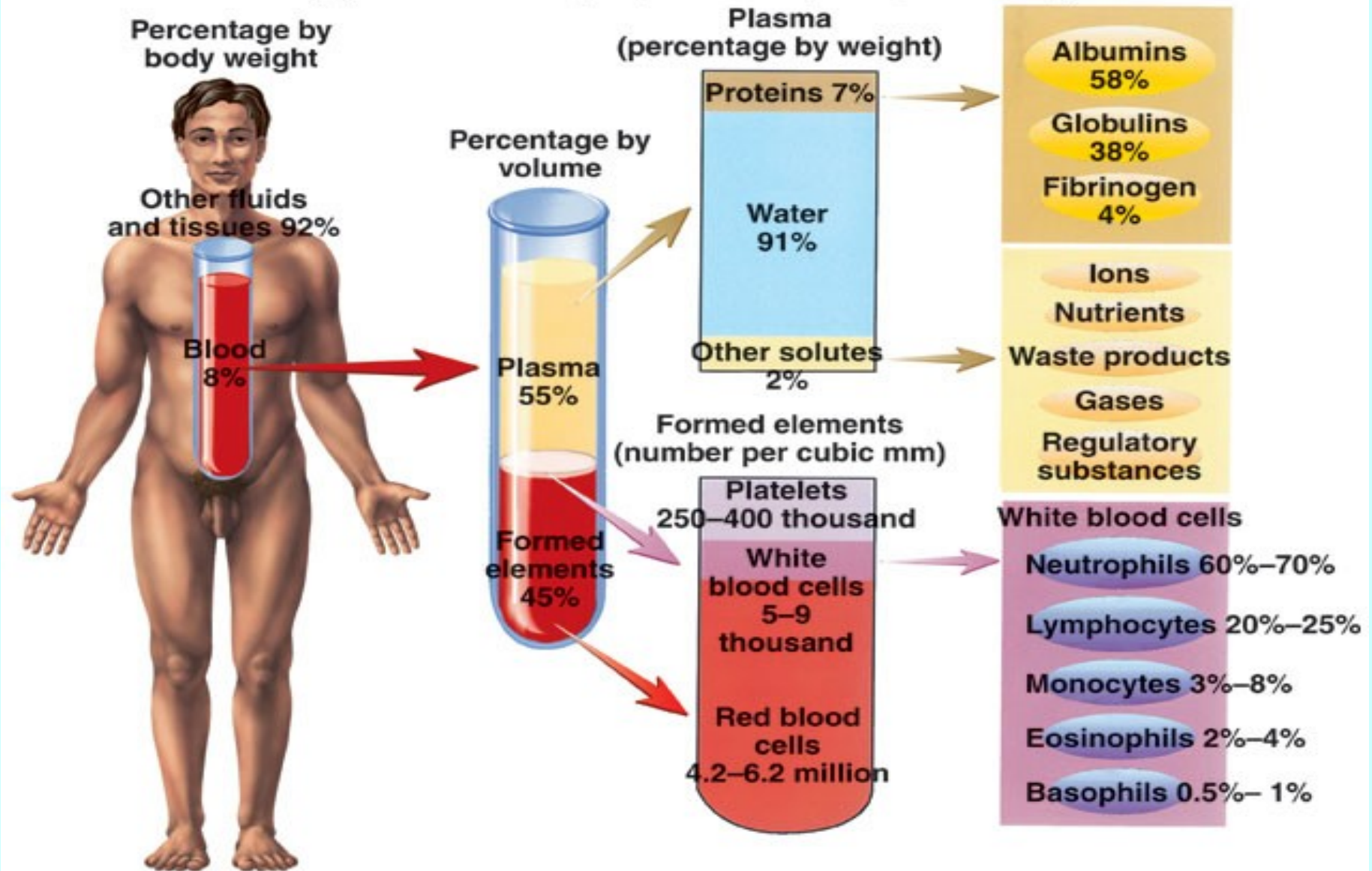


# Functions of Blood

- Transport of:
  - Gases, nutrients, waste products
  - Processed molecules
  - Regulatory molecules
- Regulation of pH and osmosis
- Maintenance of body temperature
- Protection against foreign substances
- Clot formation

# Composition of Blood

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# Plasma

- Liquid part of blood
  - Pale yellow made up of 91% water, 9% other
- Colloid: Liquid containing suspended substances that don't settle out
  - Albumin: Important in regulation of water movement between tissues and blood
  - Globulins: Immune system or transport molecules
  - Fibrinogen: Responsible for formation of blood clots

# Formed Elements

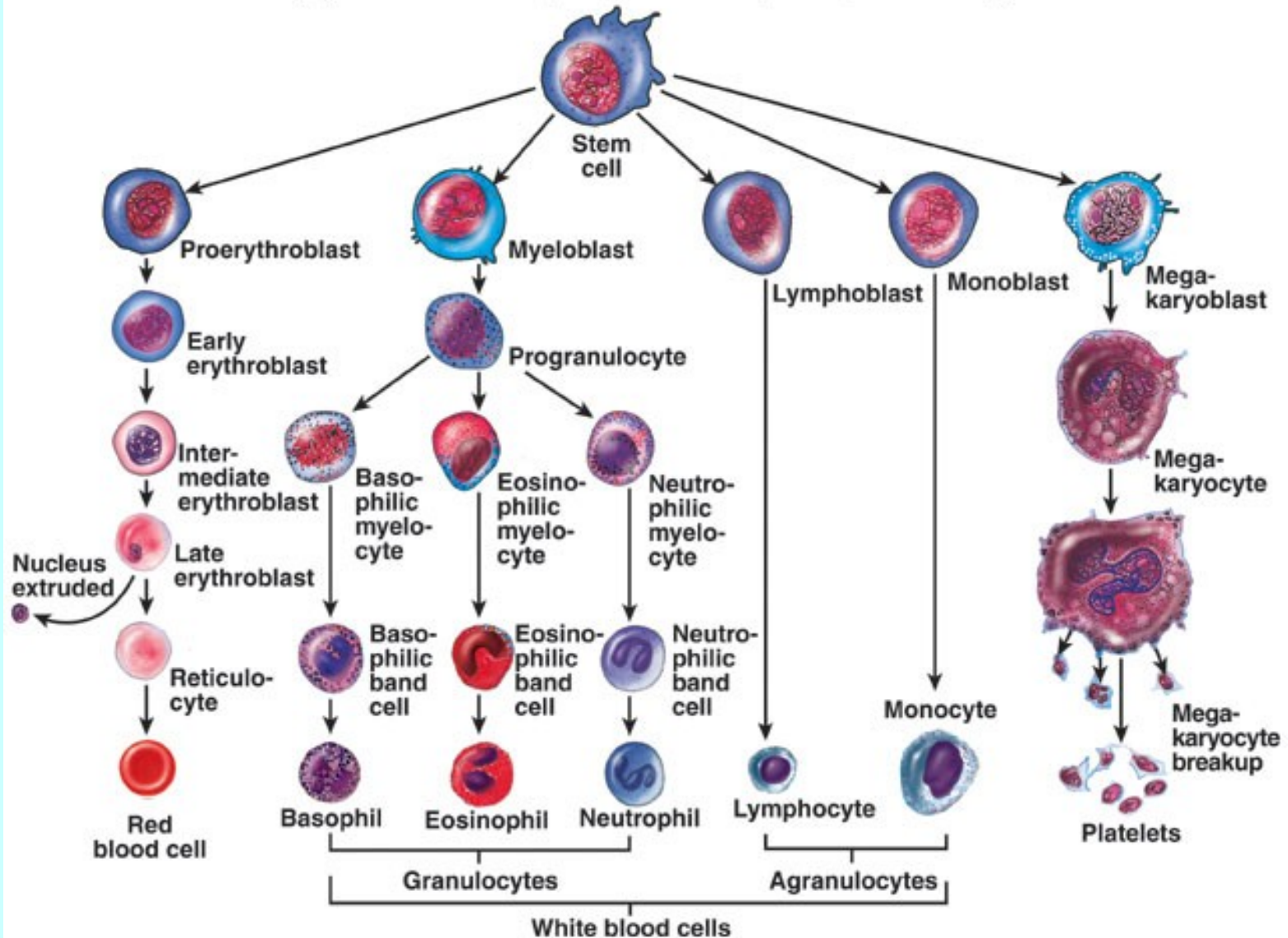
- Red blood cells (erythrocytes)
- White blood cells (leukocytes)
  - Granulocytes
    - Neutrophils
    - Eosinophils
    - Basophils
  - Agranulocytes
    - Lymphocytes
    - Monocytes
- Platelets (thrombocytes)

# Production of Formed Elements

- **Hematopoiesis or hemopoiesis:** Process of blood cell production
- **Stem cells:** All formed elements derived from single population
  - **Proerythroblasts:** Develop into red blood cells
  - **Myeloblasts:** Develop into basophils, neutrophils, eosinophils
  - **Lymphoblasts:** Develop into lymphocytes
  - **Monoblasts:** Develop into monocytes
  - **Megakaryoblasts:** Develop into platelets

# Hematopoiesis

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# Hematopoiesis;

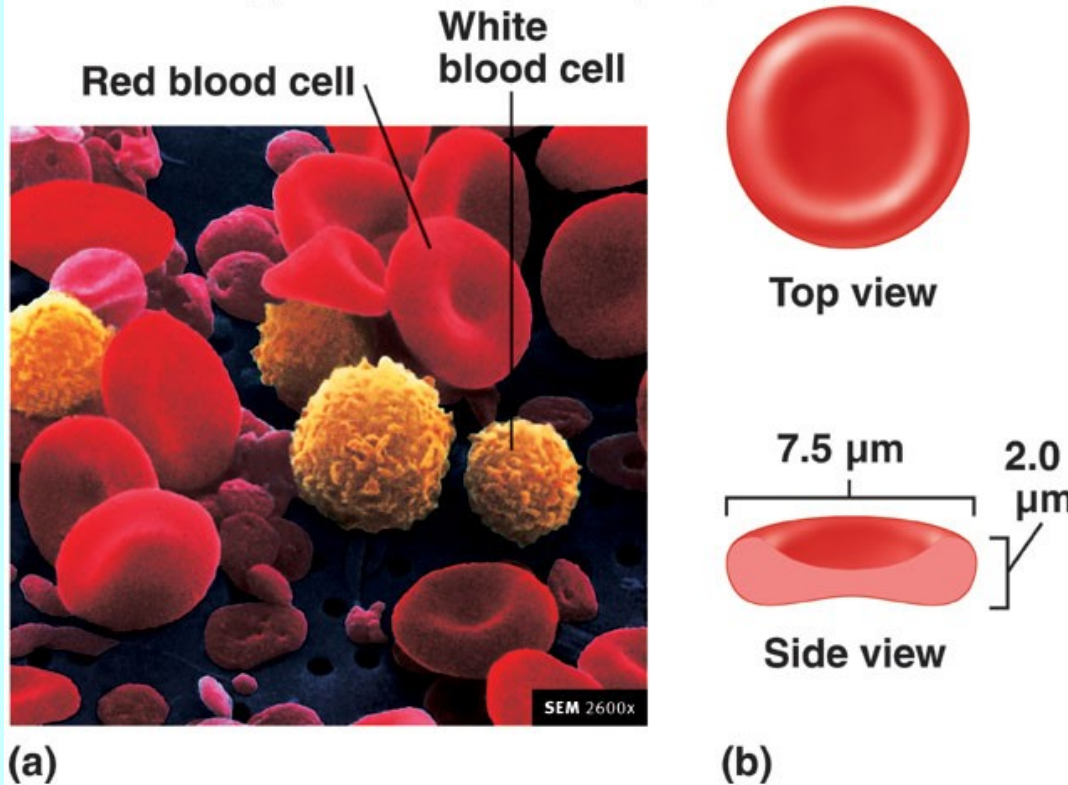
## Erythropoiesis

- Haematopoiesis describes the production of cells that circulate in the bloodstream. Specifically, erythropoiesis is the process by which red blood cells (erythrocytes) are produced.
- On average, the body produces an astounding 2.5 billion red cells/kg/day. Erythrocytes arise from a complex line of cells, and their rate of production is tightly regulated to ensure adequate



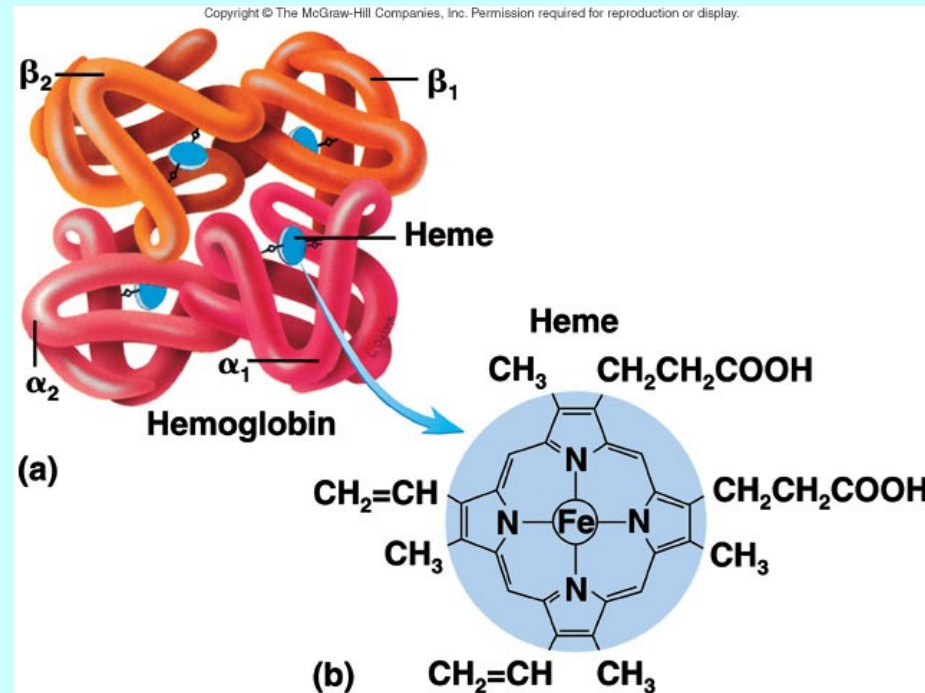
# Erythrocytes

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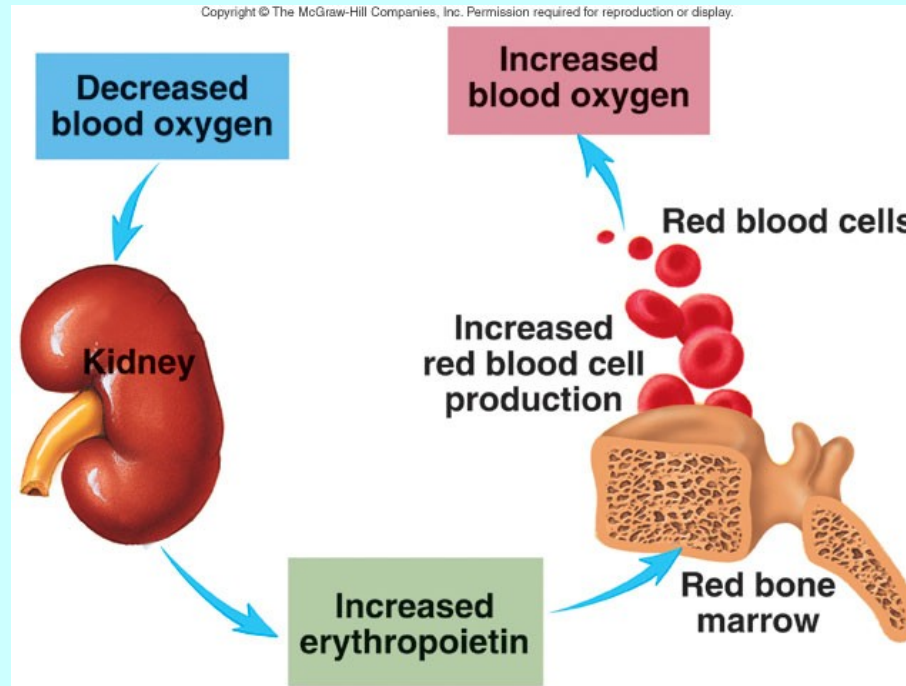
- Structure
  - Biconcave, anucleate
- Components
  - Hemoglobin
  - Lipids, ATP, carbonic anhydrase
- Function
  - Transport oxygen from lungs to tissues and carbon dioxide from tissues to

# Hemoglobin



- Consists of:
  - 4 globin molecules: Transport carbon dioxide (carbonic anhydrase involved), nitric oxide
  - 4 heme molecules: Transport oxygen
    - Iron is required for oxygen transport

# Erythropoiesis



- Production of red blood cells
  - Stem cell → proerythroblasts → early erythroblasts → intermediate → late reticulocytes
- **Erythropoietin:** Hormone to stimulate RBC production

# Sites of erythropoiesis

- The site of erythropoiesis changes throughout life. In the very early foetus, it occurs in the yolk sac. From 2 - 5 months gestation, it occurs in the liver and spleen before finally establishing in the bone marrow from about 5 months gestation.
- In children, erythropoiesis can occur in the bone marrow of most bones. However, in adults, it only occurs in the bone marrow of the vertebrae,

# Sites of erythropoiesis

- When erythropoiesis is inadequate in the bone marrow, this can trigger extramedullary haematopoiesis – i.e. haematopoiesis occurring outside the marrow. This is commonly seen in haemoglobinopathies such as thalassaemias and myelofibrosis.

# Regulation of Erythropoiesis

- Erythropoiesis is driven mainly by the hormone erythropoietin (EPO), which is a glycoprotein cytokine.
- EPO is secreted by the kidney. It is constantly secreted at a low level, sufficient for the normal regulation of erythropoiesis. However, if the erythrocyte level becomes inadequate, the blood becomes relatively hypoxic. When there is a reduced partial pressure of oxygen ( $pO_2$ ) in the kidney, this is detected

# Clinical Relevance

- Chronic kidney disease often causes anaemia. In the damaged kidney, there is a reduced basal level EPO production and a reduced response to hypoxia leading to anaemia. To counteract this, patients can be given EPO injections as required.
- Drug Doping -Exogenous EPO can be used as a performance-enhancing drug among athletes. By stimulating increased red blood cell production, it increases the amount of haemoglobin available for oxygen binding, thus improving the oxygen supply to muscles. However, studies have disagreed

# Clinical Relevance

- Underproduction of Red Blood Cells
- The underproduction of red blood cells results in anaemia. Anaemia is defined as a low haemoglobin concentration, but the absolute values differ between women and men
- In broad terms, anaemia can be caused by decreased red cell production, or increased red cell removal. Here we will briefly consider the causes of decreased red

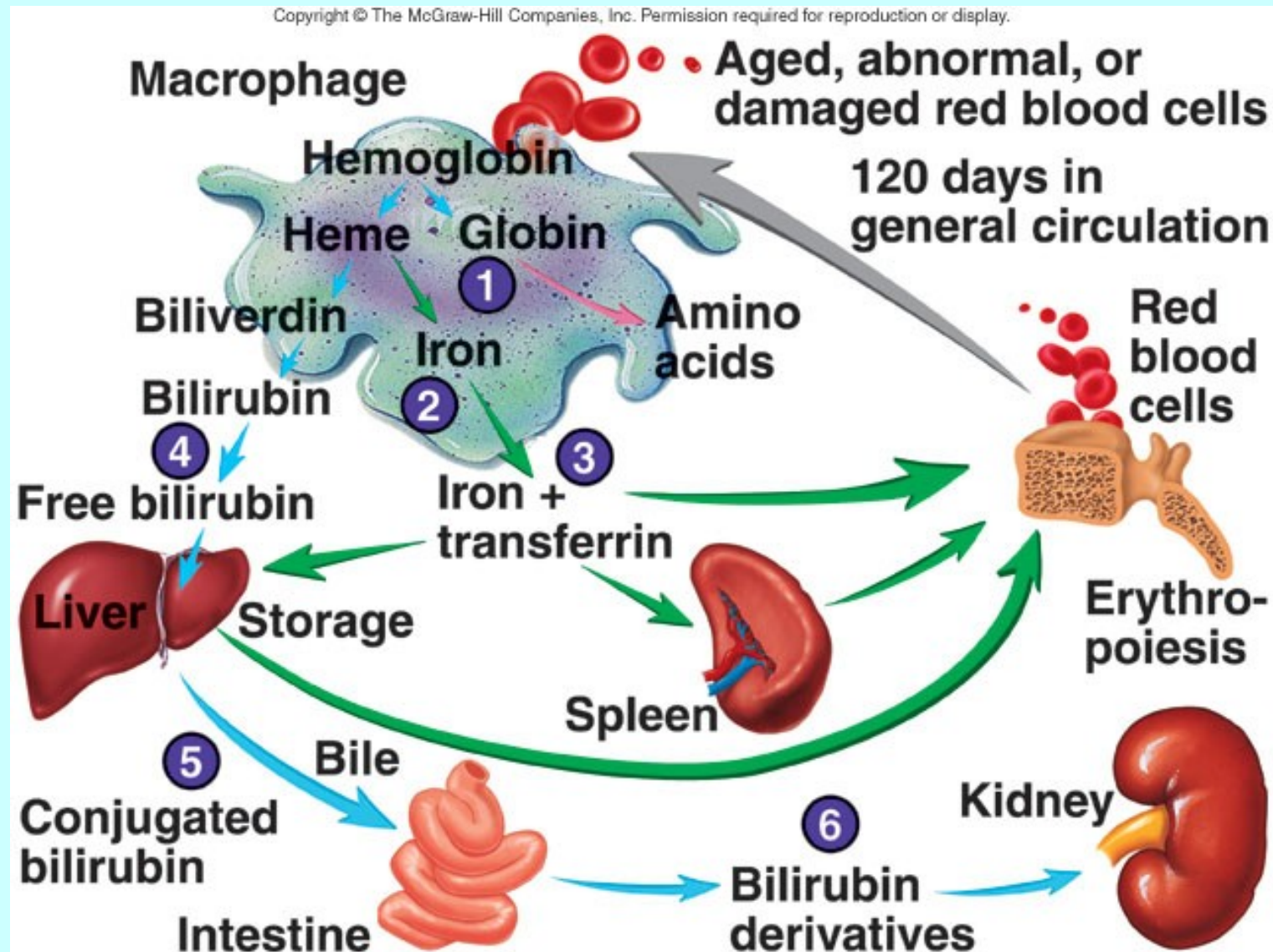


# Clinical Relevance

Reduced red cell production may be due to 3 main things:

- Lack of 'building blocks' for production, e.g. iron, folate or B12 deficiency.
- Failure of the stimulus – i.e. EPO deficiency secondary to chronic kidney disease.
- Bone marrow failure, such as aplastic anaemia.
- Clinical Relevance – Overproduction of Red Blood Cells
- Overproduction of red blood cells can occur in conditions such as polycythaemia rubra vera. This is a myeloproliferative disease

# Hemoglobin Breakdown



# Hemoglobin Breakdown

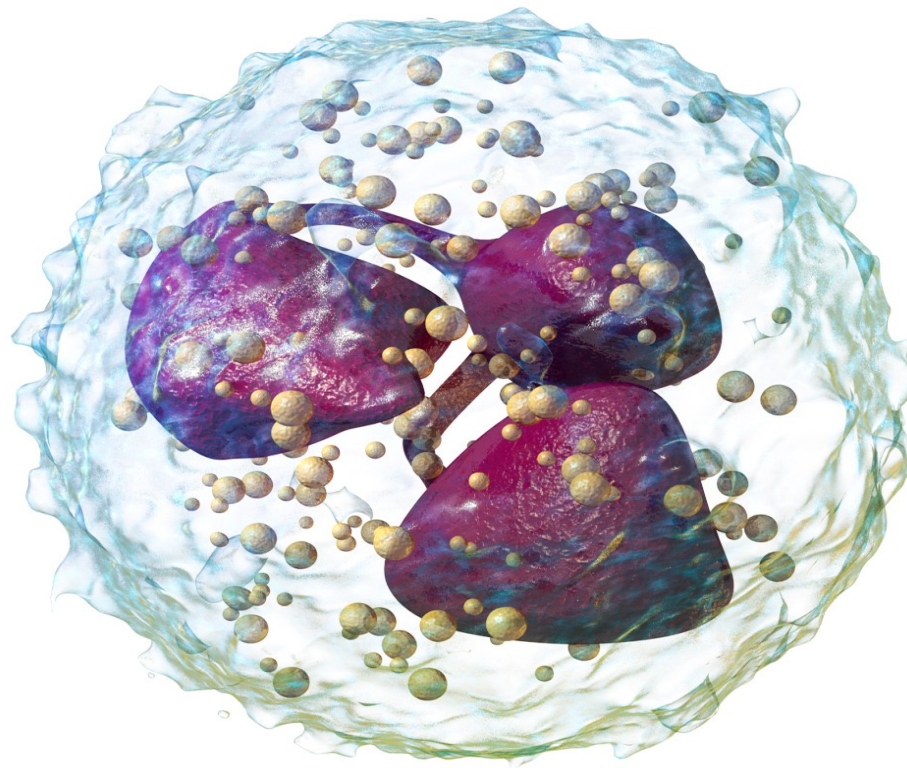
- Hemoglobin is initially broken down inside macrophages and the heme groups are separated from the globin chains. The globin chains are subsequently catabolized into amino acid residues which can be recycled to make other new proteins.
- Next, ferrous iron ( $\text{Fe}^{2+}$ ) is removed from the heme ring and leaves the macrophage by way of

# Hemoglobin Breakdown

- Ferric iron binds to the protein transferrin in the blood and most of it is transported to the bone marrow to be used again in erythropoiesis to form new red blood cells.
- With iron gone, the remaining heme ring is quickly oxidized to become biliverdin, which is bluish-green in color. Biliverdin then goes through another biochemical transformation to become unconjugated bilirubin, which is yellow in color. It is then released into the

# Leukocytes

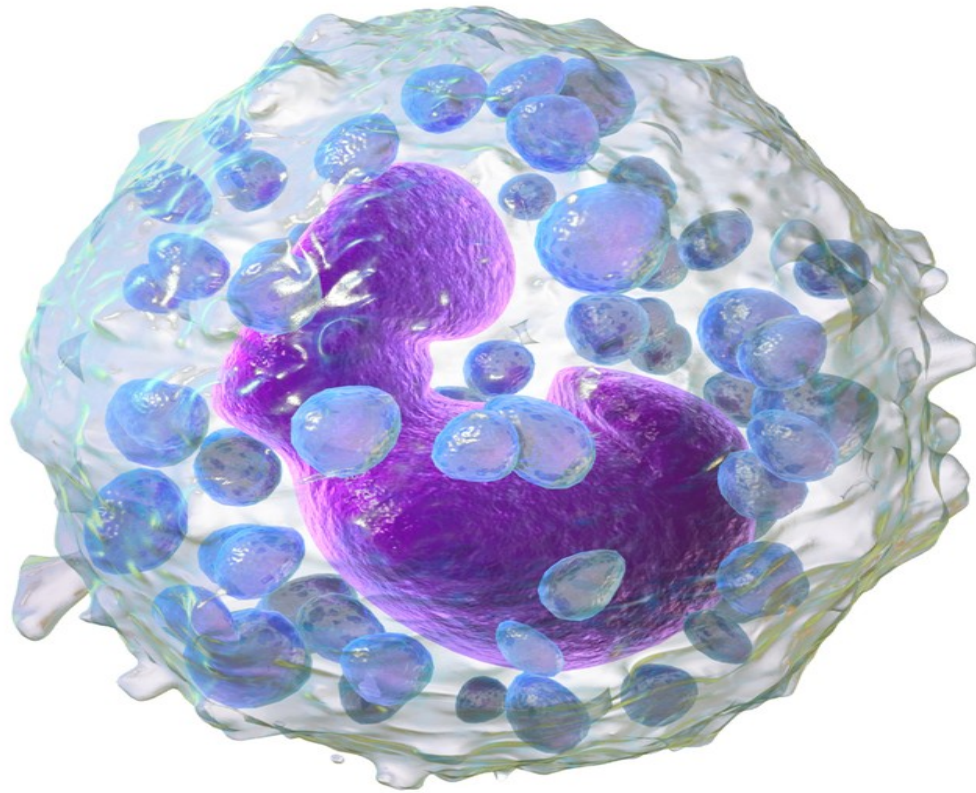
- Protect body against microorganisms and remove dead cells and debris
- Movements
  - Ameboid
  - Diapedesis
  - Chemotaxis
  - Passive Immunity
  - Active Immunity
  - Antigen - Antibody
- Types
  - **Neutrophils**: Most common; phagocytic cells destroy bacteria (60%)
  - **Eosinophils**: Detoxify chemicals; reduce inflammation (4%)
  - **Basophils**: Allergic reactions; Release histamine, heparin increase inflam. response (1%)
  - **Lymphocytes**: Immunity 2 types; b & t Cell types. IgG-infection, IgM-microbes, IgA-Resp & GI, IgE- Allergy, IgD-immune response



**Neutrophil**



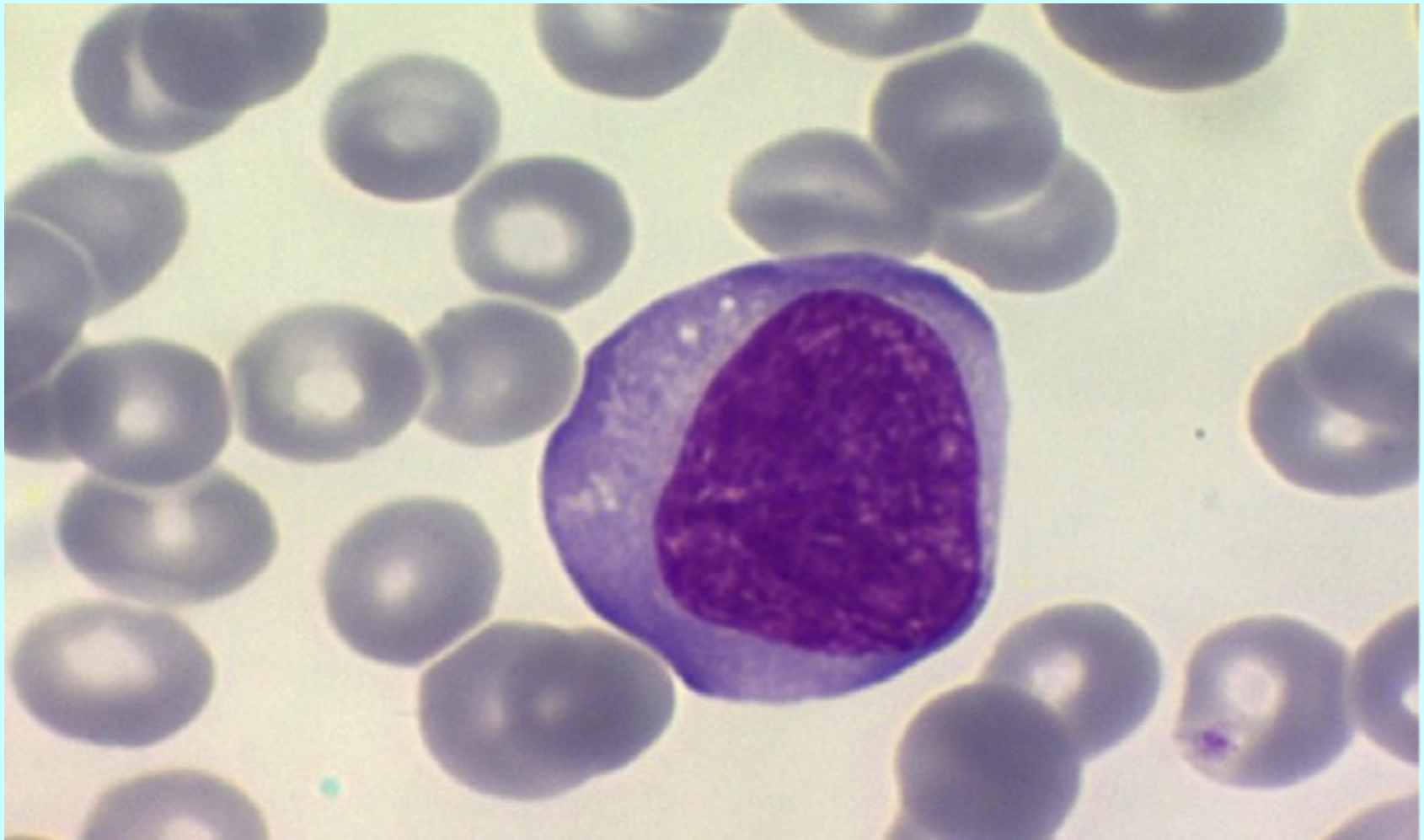




**Basophil**



# Lymphocytes

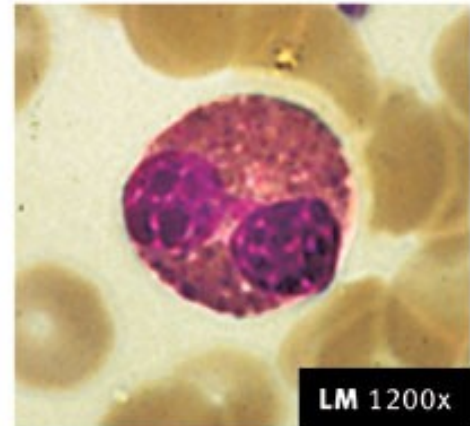
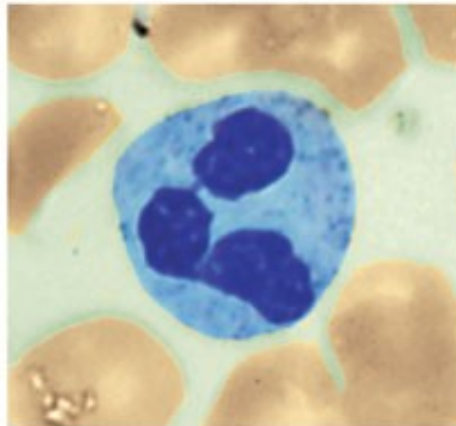
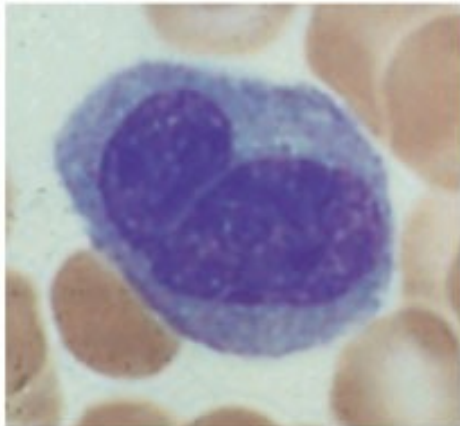
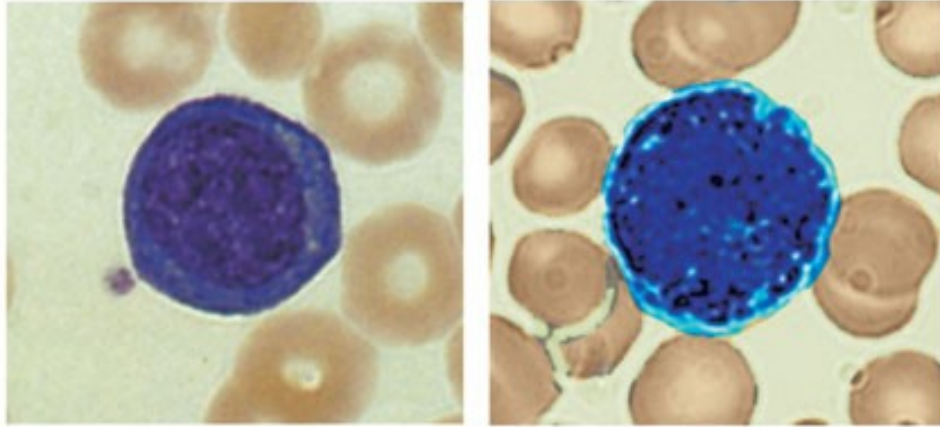


# Monocytes



# Leukocytes

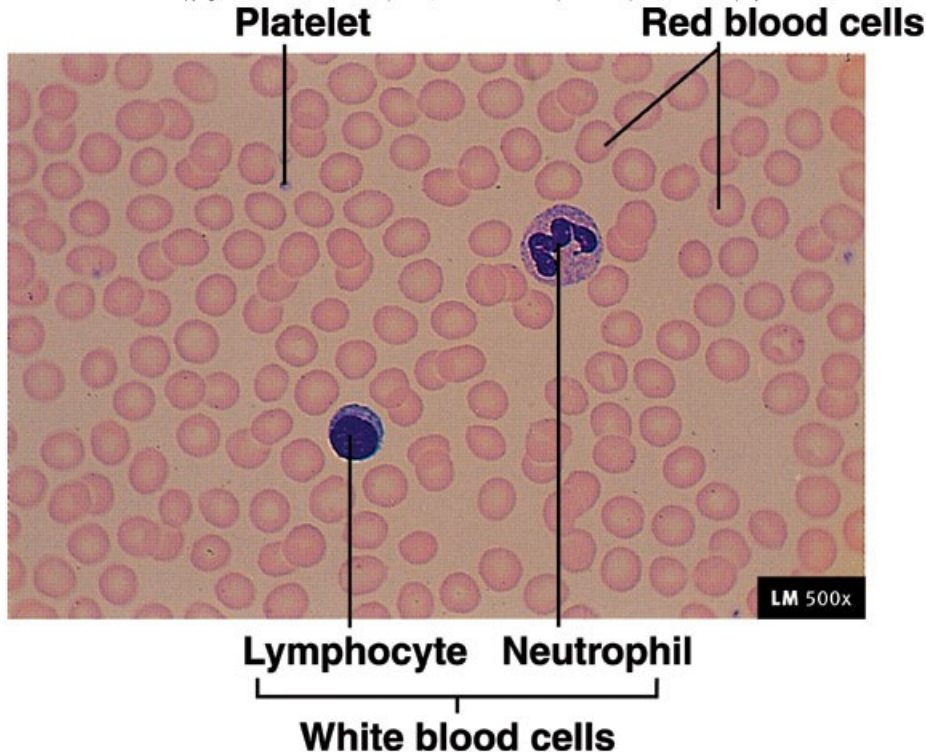
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LM 1200x

# Thrombocytes

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- Cell fragments pinched off from megakaryocytes in red bone marrow
- Important in preventing blood loss
  - Platelet plugs
  - Promoting formation and contraction of platelets

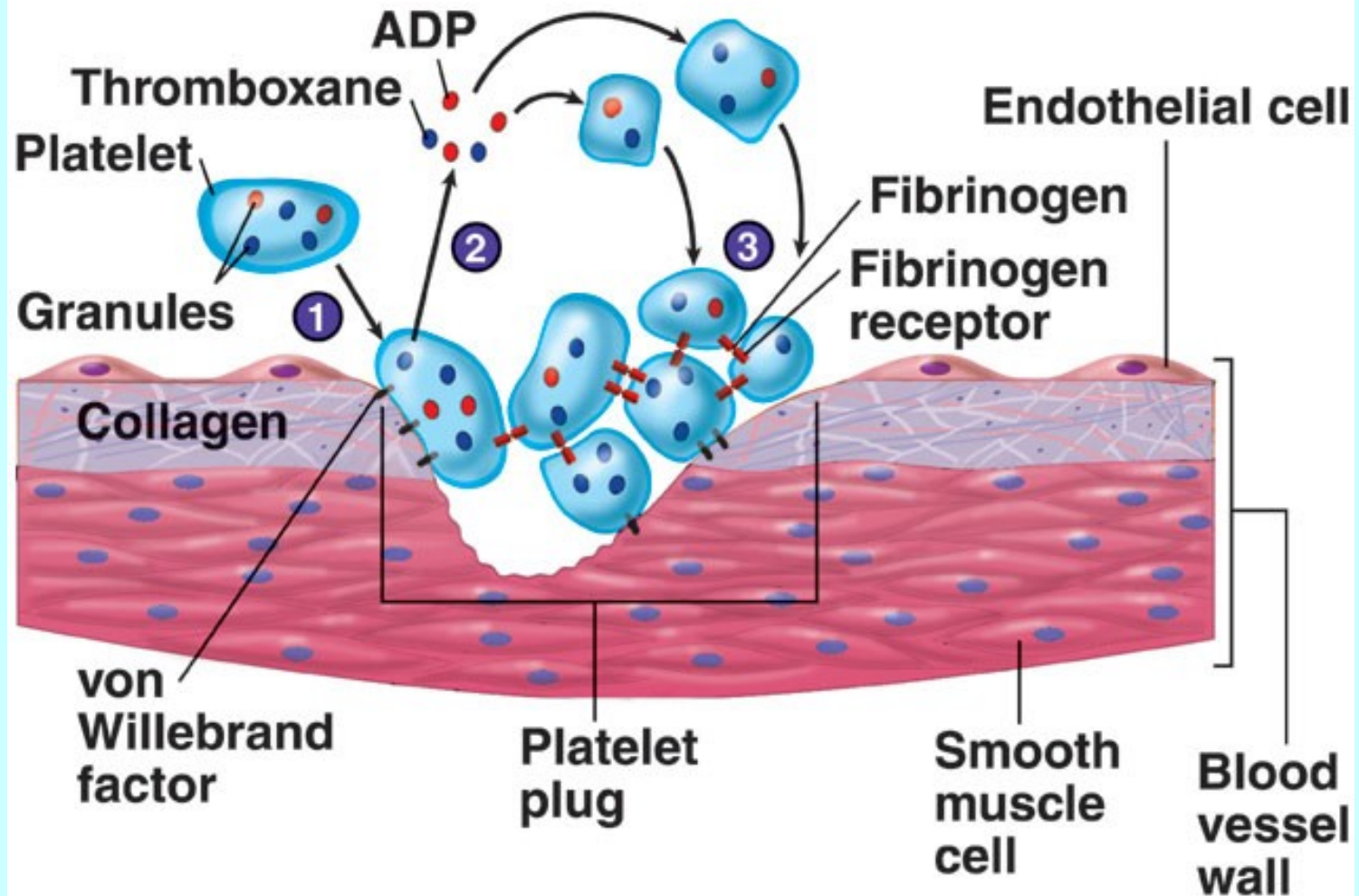
# Hemostasis

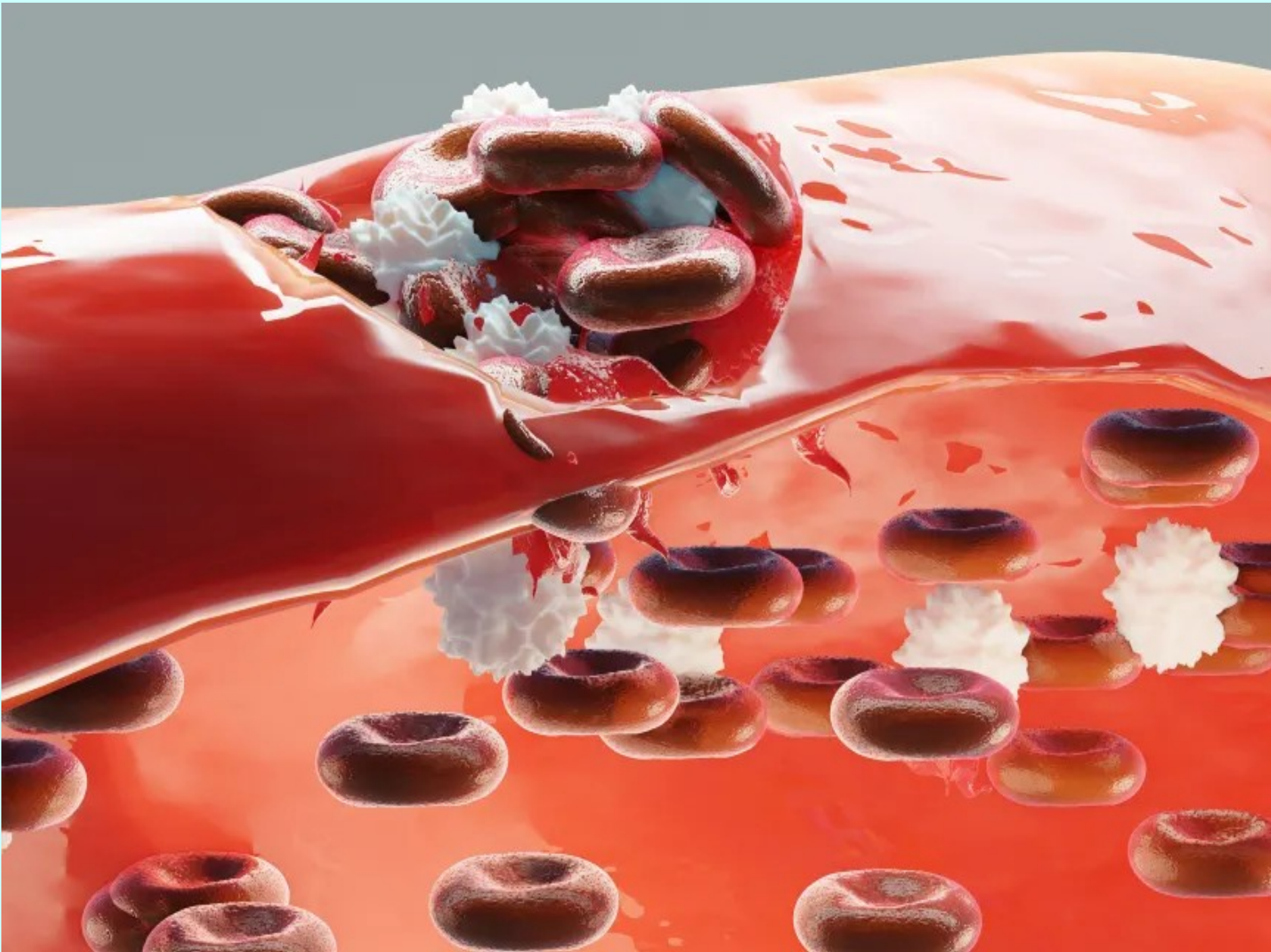
- Arrest of bleeding
- Events preventing excessive blood loss
  - **Vascular spasm**: Vasoconstriction of damaged blood vessels
  - Platelet plug formation
  - Coagulation or blood clotting



# Platelet Plug Formation

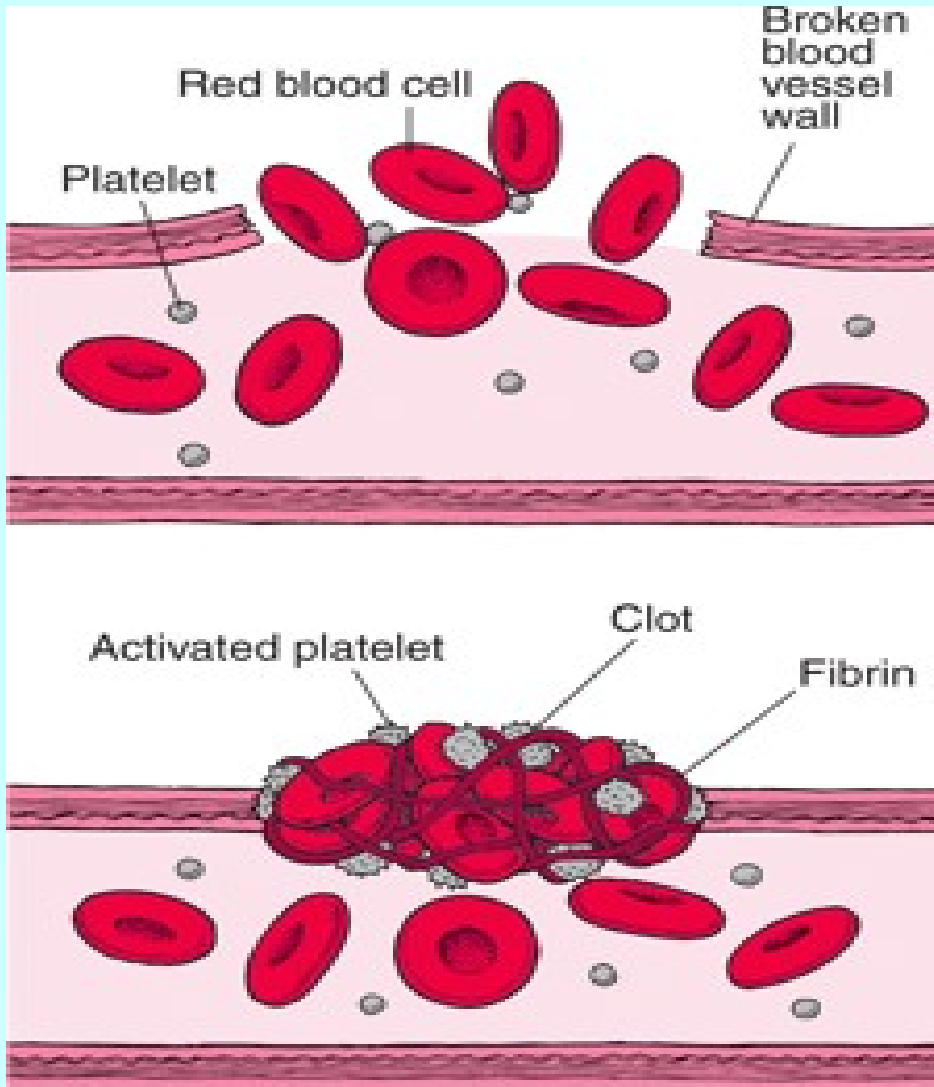
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# Coagulation



- Stages

- Activation of prothrombinase
- Conversion of prothrombin to thrombin
- Conversion of fibrinogen to fibrin

- Pathways

- Extrinsic
- Intrinsic

# Clot Formation

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**Stage 1 can be activated in two ways:**

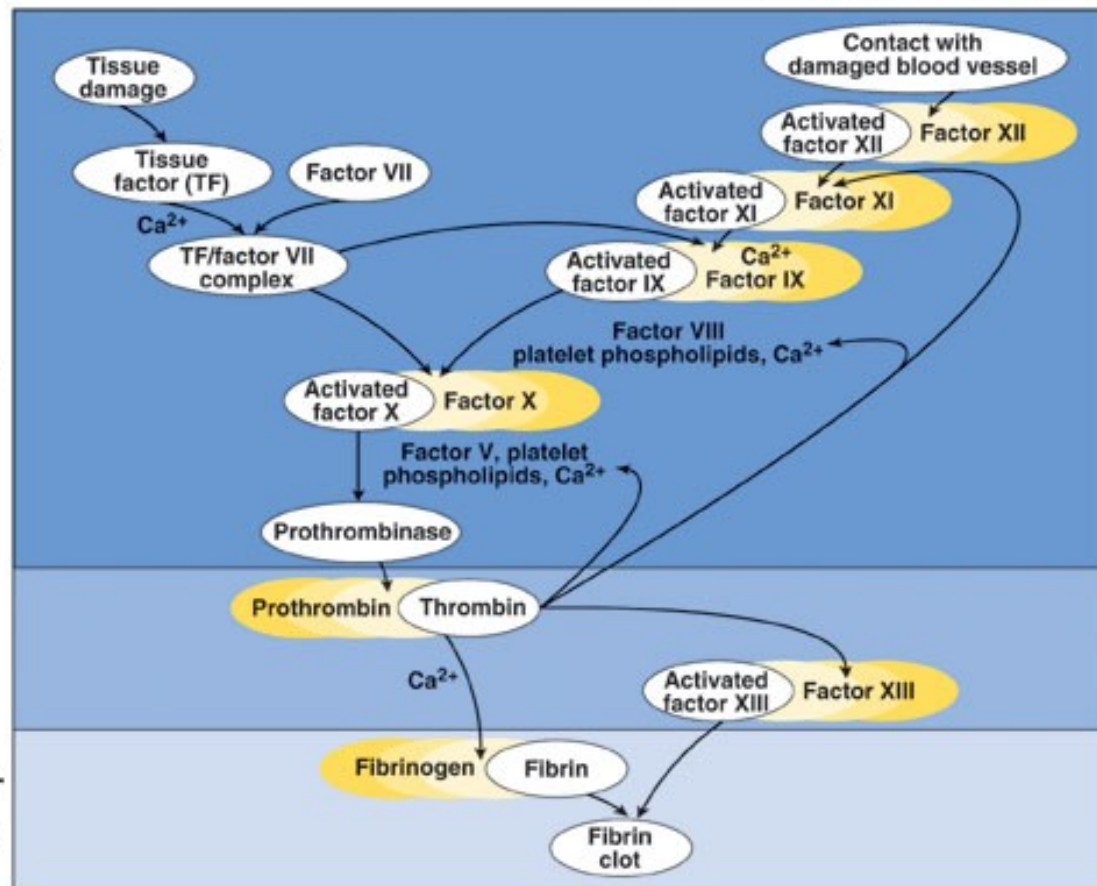
**Extrinsic clotting pathway** starts with tissue factor, which is released outside of the plasma in damaged tissue.

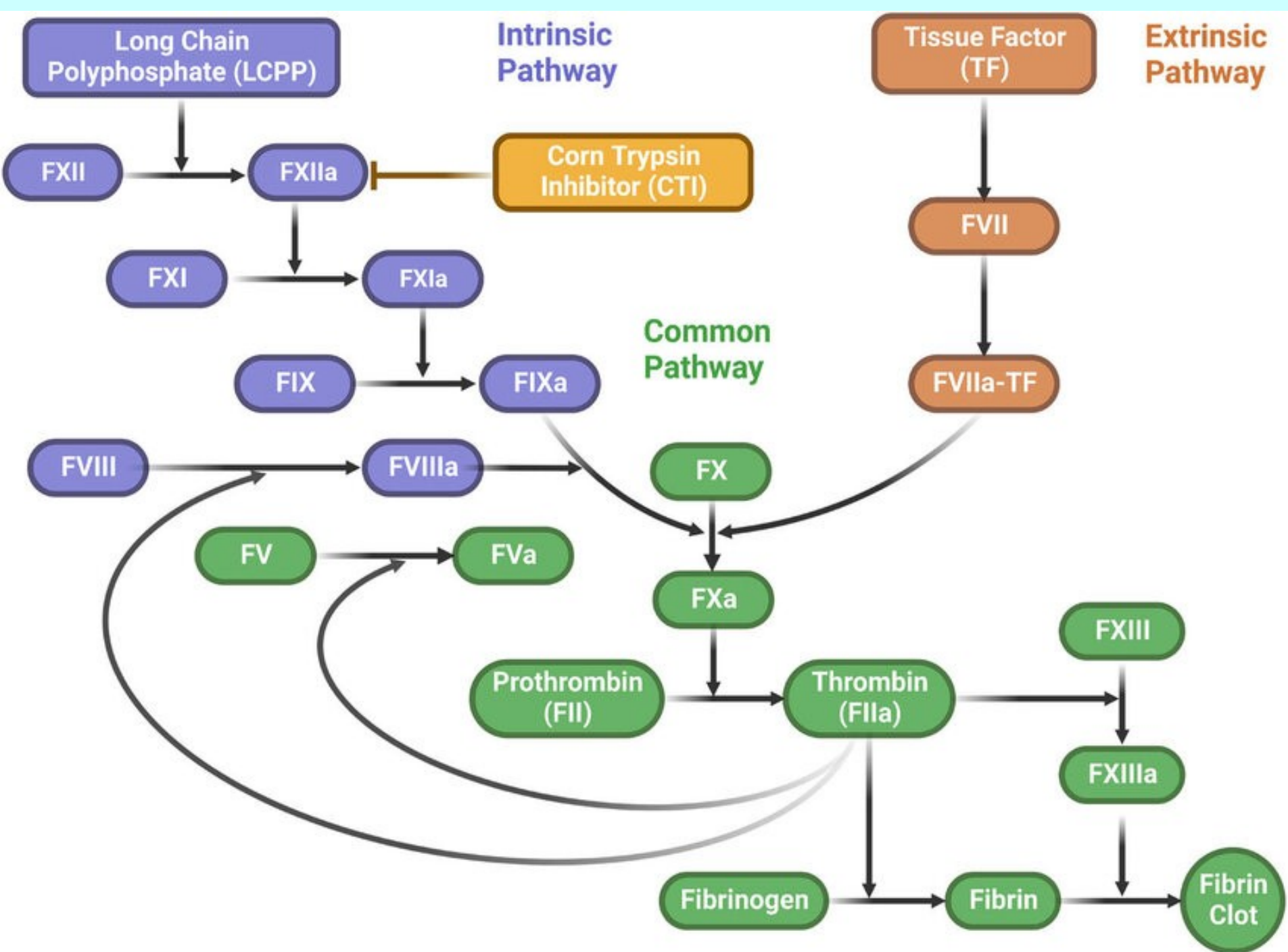
**Intrinsic clotting pathway** starts when inactive factor XII, which is in the plasma, is activated by coming into contact with a damaged blood vessel.

**Stage 1:** Damage to tissue or blood vessels activates clotting factors that activate other clotting factors, which leads to the production of prothrombinase. The activated factors are within *white ovals*, whereas the inactive precursors are shown as *yellow ovals*.

**Stage 2:** Prothrombin is activated by prothrombinase to form thrombin.

**Stage 3:** Fibrinogen is activated by thrombin to form fibrin, which forms the clot.





# **PLATELETS AND BLOOD COAGULATION**

Joseph Kamaloni & Lweendo  
Mapani

❑ What is blood coagulation?

❑ Why is it important ?

❑ How does it happen?

❑ What are platelets?

❑ What is the role of platelets in blood coagulation?

# Formed elements

- ❑ Red blood cells (erythrocytes)
- ❑ White blood cells (leukocytes)
- ❑ **Platelets**  
**(thrombocytes)**

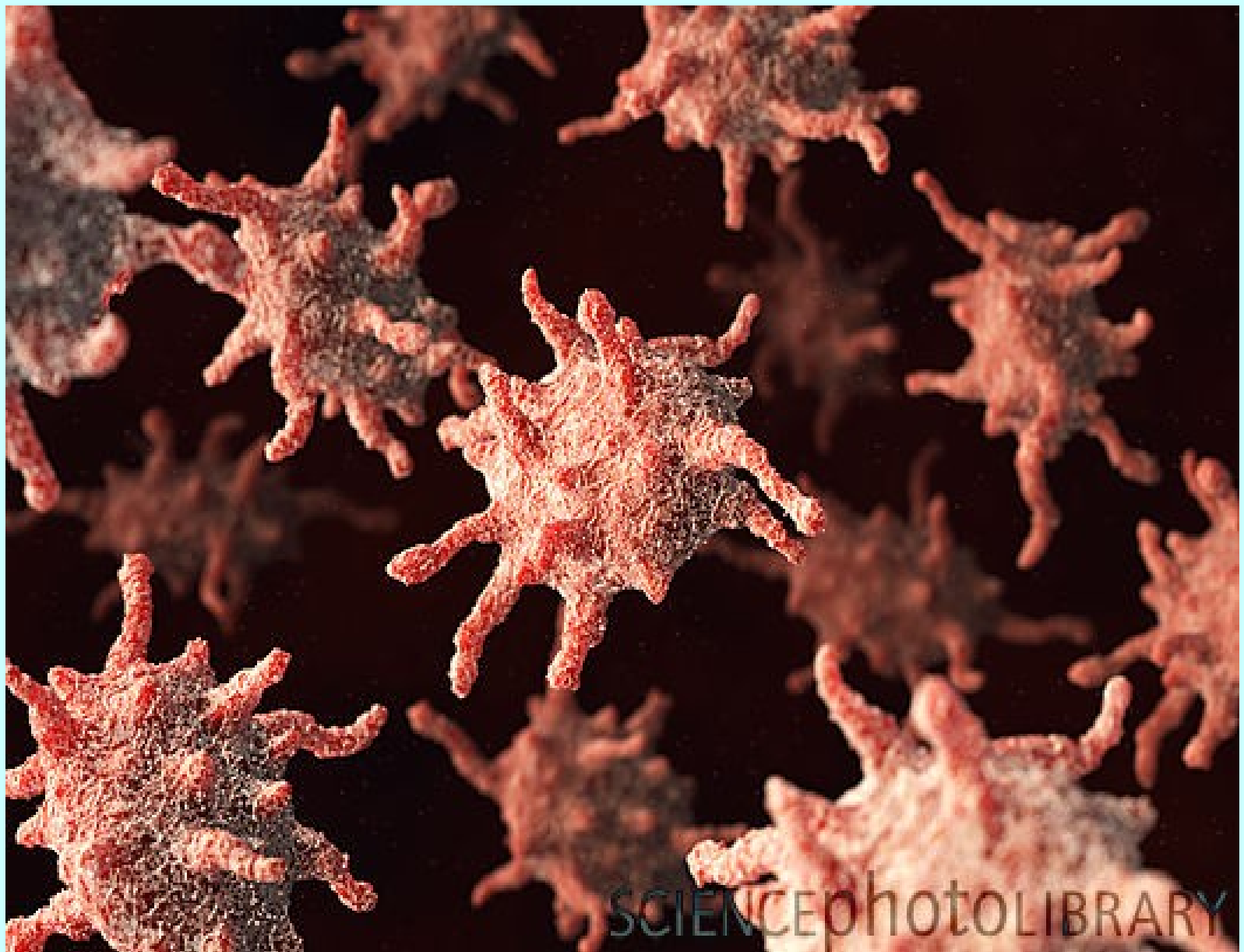


## **Platelets (thrombocytes)**

- ❑ Small granulated bodies that aggregate at sites of vascular injury
- ❑ Have no nucleus
- ❑ 2 - 4 micrometer in diameter
- ❑ 300,000 per micro liter of blood
- ❑ Life span is about 7 - 10 days

# **Platelets (thrombocytes)**

- ❑ Formed in the bone marrow by megakaryocytes ,giant cells in bone marrow
- ❑ 60% - 75% are in circulating blood
- ❑ The remainder mostly in the spleen
- ❑ Splenectomy – thrombocytosis



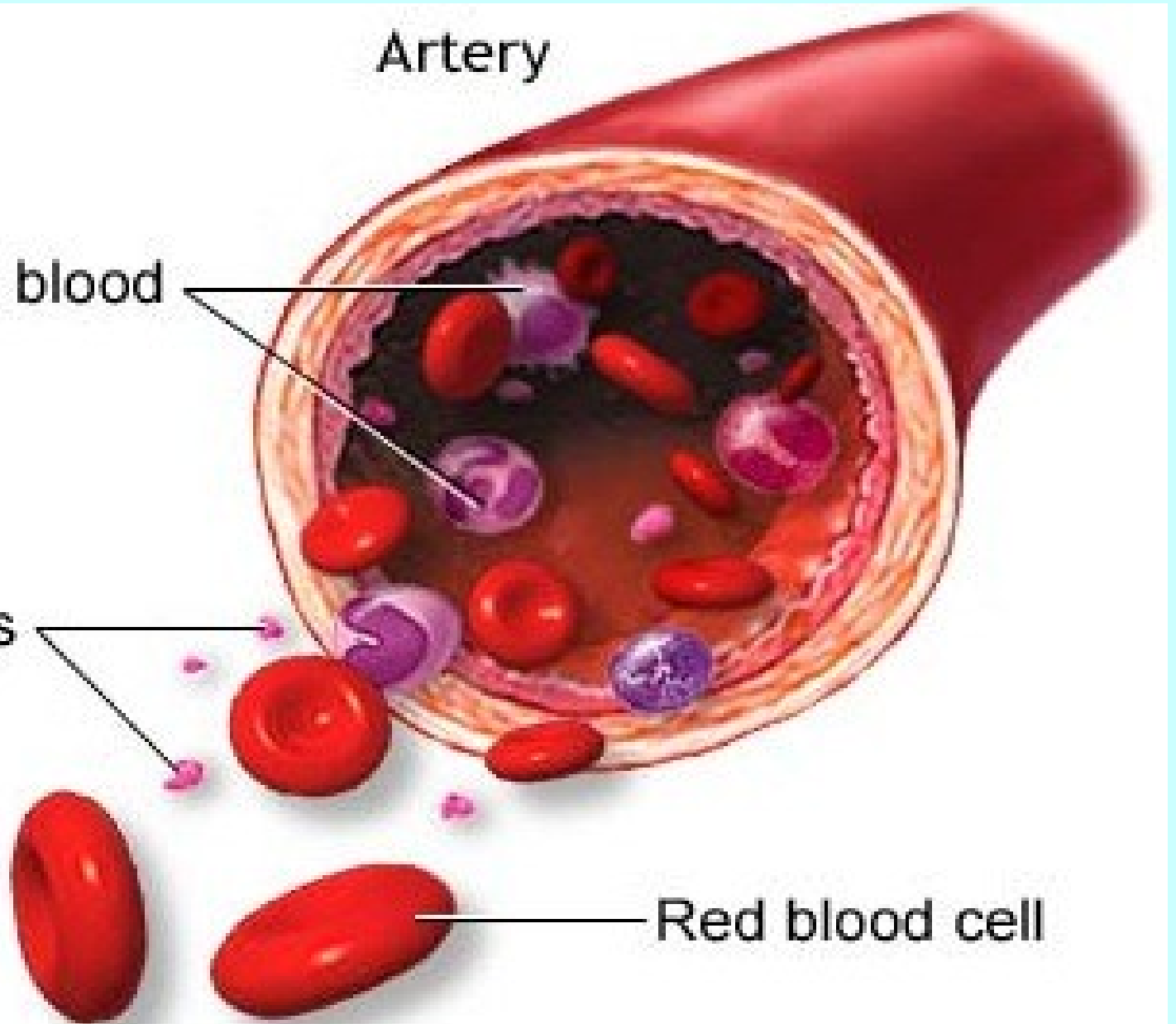
SCIENCEPHOTOLIBRARY

Artery

White blood cells

Platelets

Red blood cell



# Function of platelets

- ❑ Basic to the function of platelets is their ability to stop bleeding in a case of vascular injury – **hemostasis** and its role in **COAGULATION**
- ❑ With 1 – 5 seconds after an injury, platelets adhere to the damaged epithelium and to each other – **hemostatic platelet** plug is formed

# Hemostasis

- ❑ The process of forming clots in the walls of damaged blood vessels and preventing blood loss while maintaining blood in a fluid state within the vascular system

# Response to Injury

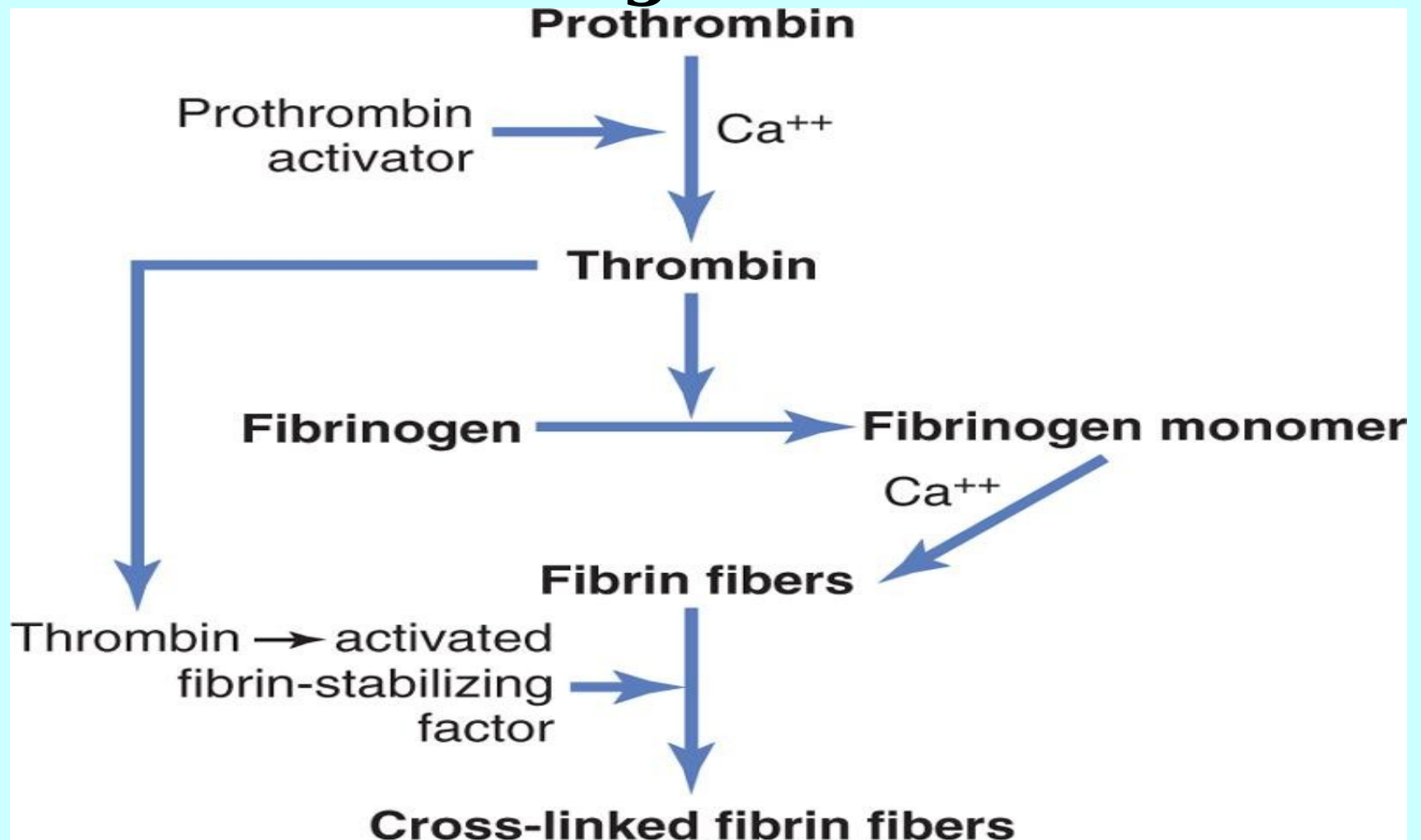
- ❑ Small blood vessel injured
- ❑ Constriction of blood vessel – due to serotonin and other vasoconstrictors liberated from platelets
- ❑ Platelets adhere to wall of damaged vessels
- ❑ A clot is formed which closes the injured vessels and stops further loss of blood



# The clotting Mechanism

- ❑ Same as coagulation
- ❑ four components critical to coagulation:
  1. Prothrombin
  2. Thrombin
  3. Fibrinogen
  4. Fibrin

# The clotting Mechanism



# **The three stages are.....**

## **Stage 2**

- ❑ Prothrombin converted to thrombin

## **Stage 3**

- ❑ Fibrinogen converted to fibrin by thrombin and calcium

# **The three stages are.....**

## **Stage 1:**

❑ Divided into two mechanisms;

a) Extrinsic pathway and

b) Intrinsic pathway

## Stage 1

- ❑ In both pathways a series of chemical reactions called a **clotting cascade** precedes the formation of Prothrombin activator (substance needed for conversion of Prothrombin to thrombin)

# Stage 1

- ❑ In **extrinsic pathway** chemicals that trigger the cascade events are extrinsic to the blood i.e. outside of blood
- ❑ Damage to tissue cause release of Tissue Factor (TF), or factor III which in turn acts with other factors such as factor V,VII and calcium ions
- ❑ This complex then activates factor X and produce Prothrombin activator

# Stage 1

- ❑ In **intrinsic pathway** chemicals that trigger the cascade events normally present, or intrinsic, to the blood
- ❑ Damage of the endothelial lining of blood vessels exposes collagen fibers
- ❑ Collagen fibers cause the activation of **coagulation factors** present in blood



# Stage 1

- ❑ Factor XII (Hageman factor) cause factor XI to activate factor IX to factor X
- ❑ Note that factor XII is one of the coagulation factors found in blood
- ❑ Factor X produces the Prothrombin activator

## INTRINSIC PATHWAY



Activated factor XII

Inactive XI → Active XI<sub>a</sub>

Inactive VIII

+

Active VIII<sub>a</sub>

Inactive IX

Active IX<sub>a</sub>

Inactive X

Active X<sub>a</sub>

Prothrombin

Thrombin

Fibrinogen

Fibrin

## EXTRINSIC PATHWAY

↓ damaged endothelial cells

Factor III (Tissue Factor)

Active VII<sub>a</sub> ← Inactive VII

Inactive IX

Inactive X

Active X<sub>a</sub>

Prothrombin

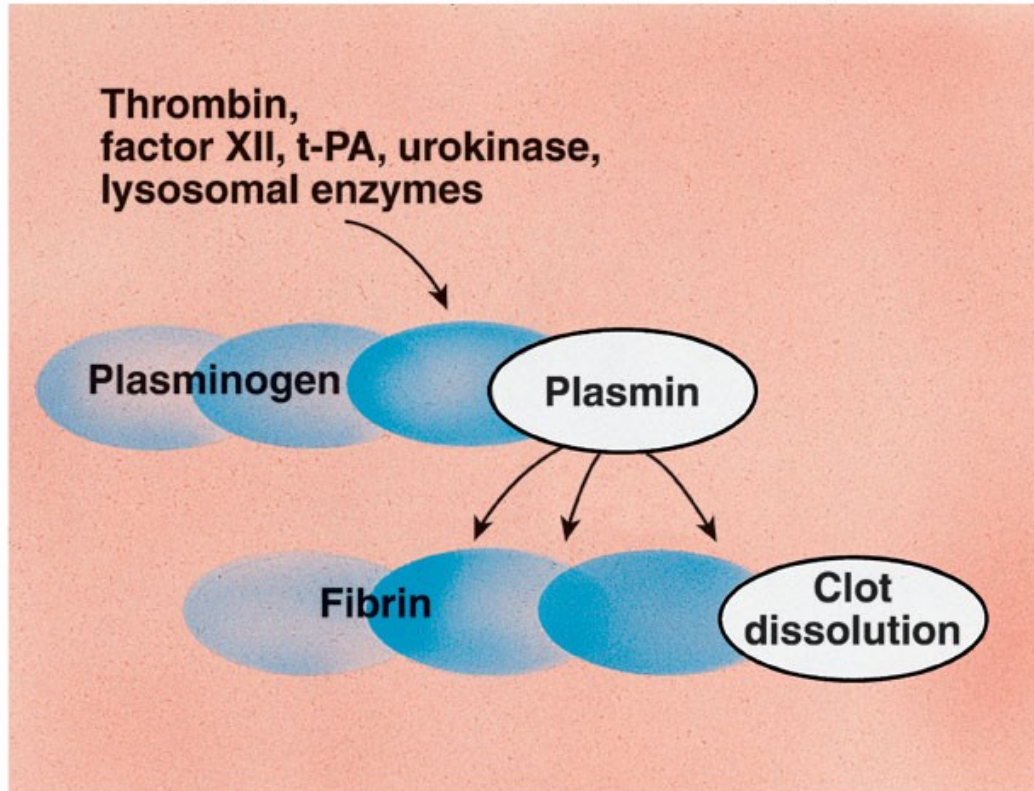
Thrombin

Fibrinogen

Fibrin

# Fibrinolysis

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- Clot dissolved by activity of plasmin, an enzyme which hydrolyzes fibrin

# Blood Grouping

- Determined by antigens (**agglutinogens**) on surface of RBCs
- Antibodies (**agglutinins**) can bind to RBC antigens, resulting in agglutination (**clumping**) or hemolysis (**rupture**) of RBCs
- Groups
  - ABO and Rh

# ABO Blood Groups

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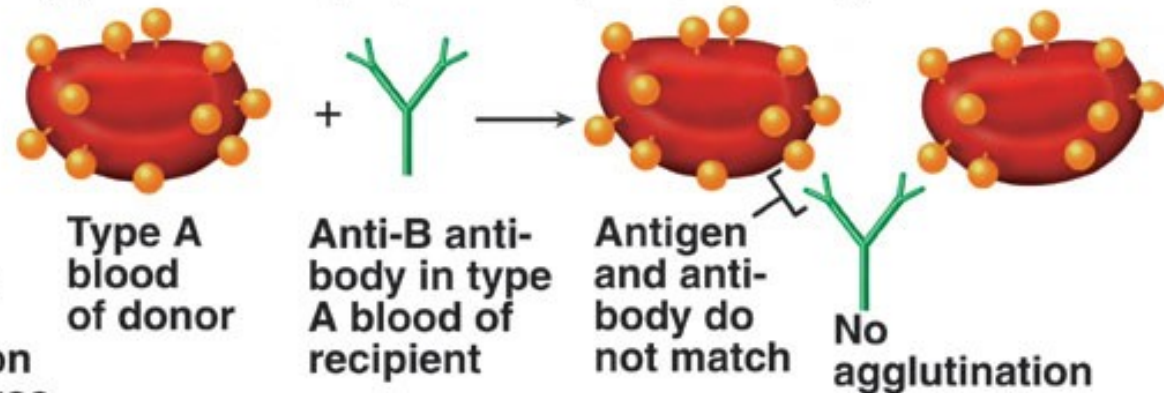
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|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|
| Red blood cells                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Antigen A<br>       | Antigen B<br>       | Antigens A and B<br> | Neither antigen A nor B<br>      |
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Anti-B antibody<br> | Anti-A antibody<br> | Neither Anti-A nor Anti-B antibodies                                                                    | Anti-A and Anti-B antibodies<br> |
| Plasma                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                      |                                                                                                       |                                                                                                         |                                                                                                                     |
| <div> <div>Type A</div> <div>Red blood cells with type A surface antigens and plasma with anti-B antibodies</div> </div> <div> <div>Type B</div> <div>Red blood cells with type B surface antigens and plasma with anti-A antibodies</div> </div> <div> <div>Type AB</div> <div>Red blood cells with both anti-A and anti-B surface antigens, and neither anti-A nor anti-B plasma antibodies</div> </div> <div> <div>Type O</div> <div>Red blood cells with neither type A nor type B surface antigens, but both anti-A and anti-B plasma antibodies</div> </div> |                                                                                                      |                                                                                                       |                                                                                                         |                                                                                                                     |

# Agglutination Reaction

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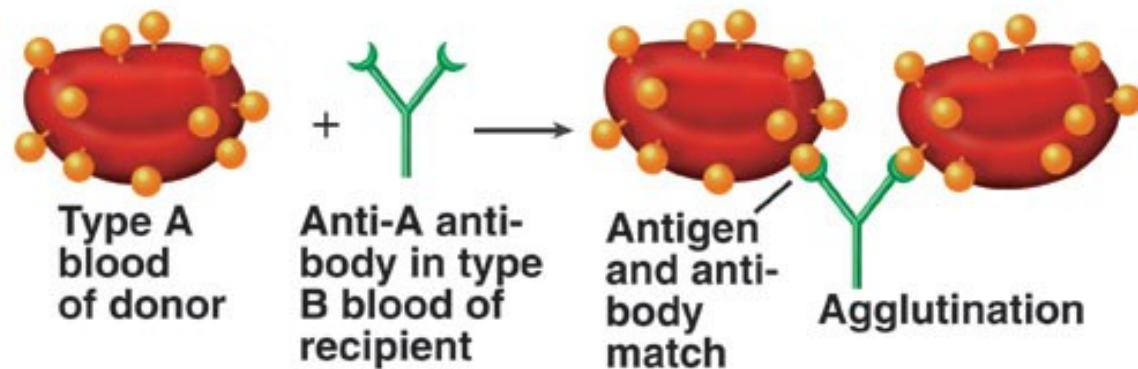
**(a) No agglutination reaction.** Type A blood donated to a type A recipient does not cause an agglutination reaction because

the anti-B antibodies in the recipient do not combine with the type A antigens on the red blood cells in the donated blood.



**(b) Agglutination reaction.** Type A blood donated to a type B recipient causes an agglutination reaction because

the anti-A antibodies in the recipient combine with the type A antigens on the red blood cells in the donated blood.



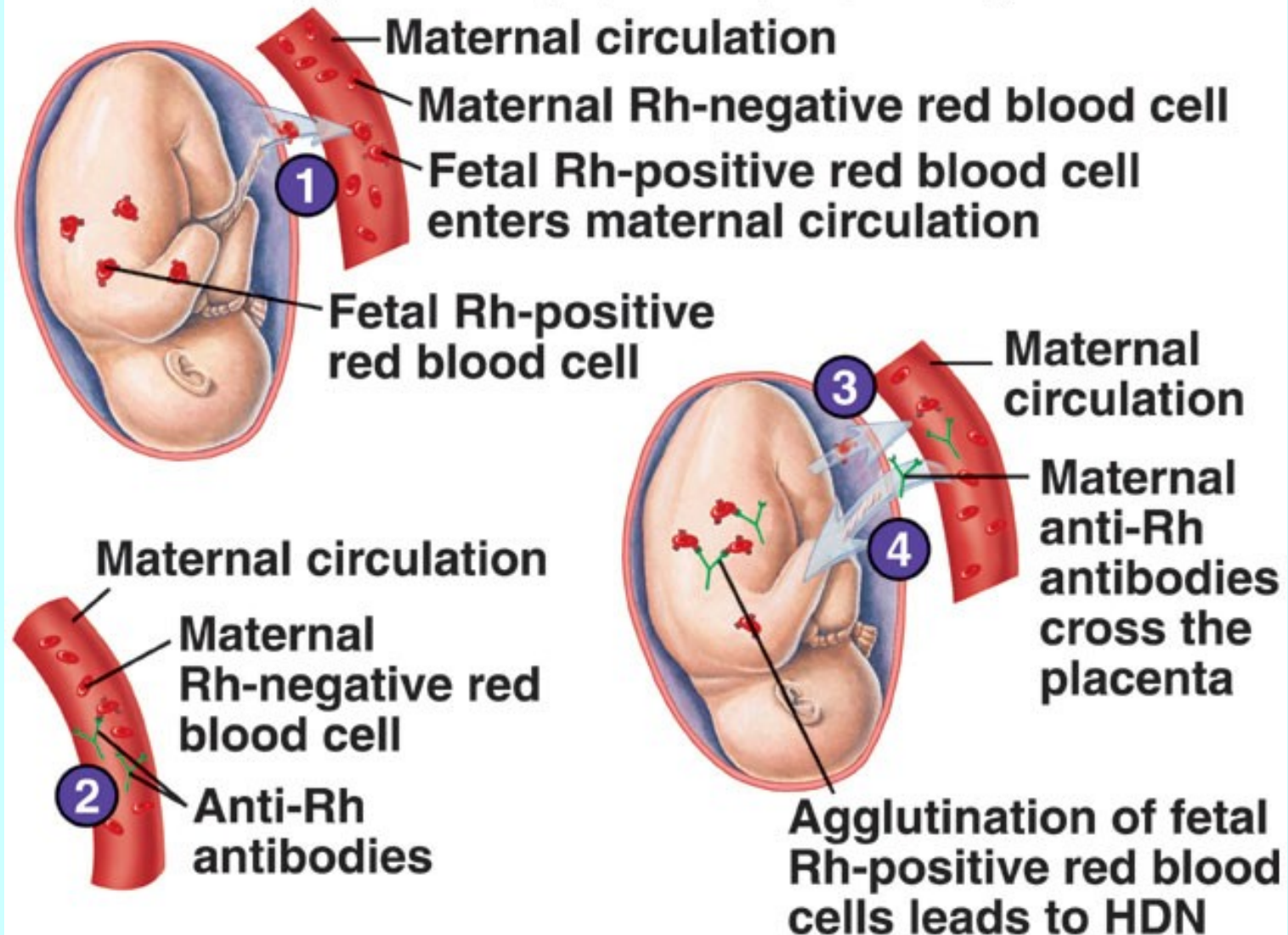
# Rh Blood Group

- First studied in rhesus monkeys
- Types
  - Rh positive: Have these antigens present on surface of RBCs
  - Rh negative: Do not have these antigens present
- Hemolytic disease of the newborn (HDN)
  - Mother produces anti-Rh antibodies that cross placenta and cause agglutination and hemolysis of fetal



# Erythroblastosis Fetalis

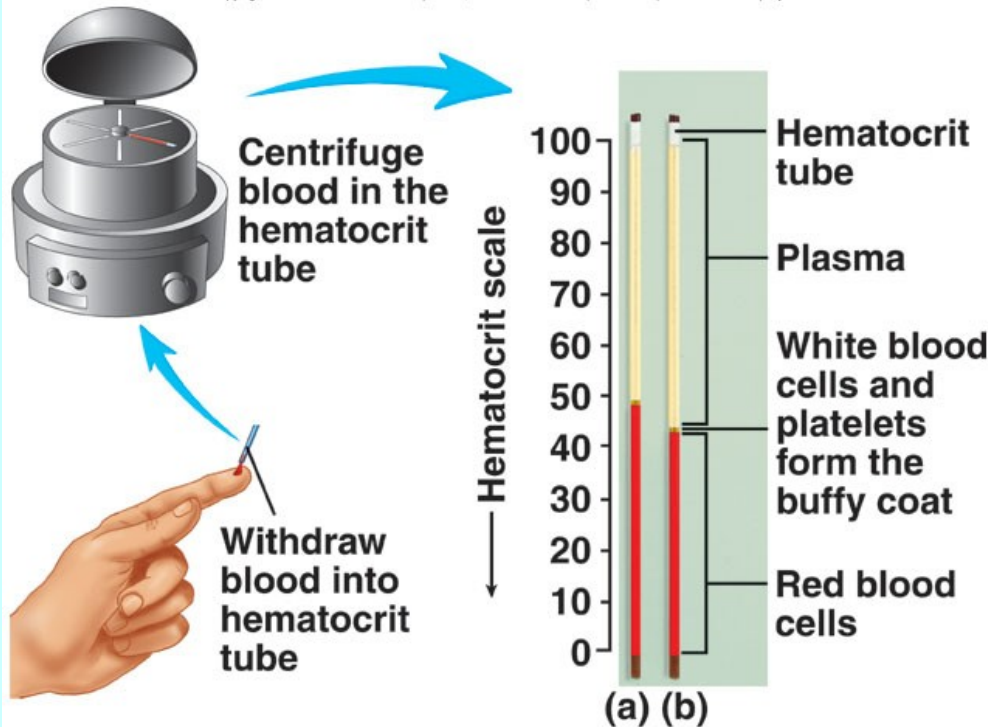
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# Diagnostic Blood Tests

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- Type and crossmatch
- Complete blood count
  - **Red blood** count
  - Hemoglobin measurement
  - Hematocrit measurement
- White blood count
- Differential white blood count

# Blood Disorders

- **Erythrocytosis:**  
RBC  
overabundance
- **Anemia:**  
Deficiency of  
hemoglobin
  - Iron-deficiency
  - Pernicious
  - Hemorrhagic
  - Hemolytic
  - Sickle-cell
- Hemophilia
- Thrombocytopenia
- Leukemia
- Septicemia
- Malaria
- Infectious  
mononucleosis
- Hepatitis

# REFERENCES

- <https://teachmephysiology.com/immune-system/haematology/erythropoiesis/>
- [https://books.byui.edu/bio\\_381\\_pathophysiol/321\\_\\_hemoglobin\\_and\\_#:~:text=Hemoglobin%20is%20initially%20broken%20down,to%20make%20other%20new%20proteins.](https://books.byui.edu/bio_381_pathophysiol/321__hemoglobin_and_#:~:text=Hemoglobin%20is%20initially%20broken%20down,to%20make%20other%20new%20proteins.)